

REMARKS

Reconsideration of the application in view of the following remarks is requested. Entry of this response is appropriate as it places the case in better condition for appeal.

I. The Rejection of Claims 1-2, 4-6, 8 and 25-29 under 35 U.S.C. 103(a)

Claims 1, 2, 4-6, 8, 25-29 were rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,017,501 to Wong (hereinafter referred to simply as "Wong") or Meier each in view of the article entitled *Polmersomes: Tough Vesicles Made of Diblock Copolymers* to Disher *et al.* (hereinafter referred to simply as "Disher") or *vice versa*, further in view of WO 97/24177. These rejections are respectfully traversed.

Obviousness is a question of law based on underlying findings of fact. An analysis of obviousness must be based on several factual inquiries: (1) the scope and content of the prior art; (2) the differences between the prior art and the claims at issue; (3) the level of ordinary skill in the art at the time the invention was made; and (4) objective evidence of nonobviousness, if any. See Graham v. John Deere Co., 383 U.S. 1, 17-18 (1966). The teachings of a prior art reference are underlying factual questions in the obviousness inquiry. See Para-Ordnance Mfg., Inc. v. SGS Imp. Int'l, Inc., 73 F.3d 1085, 1088 (Fed. Cir. 1995).

Applicants created novel detergent and surfactant containing formulations and methods which include polymersomes. These novel formulations contain vesicles that remain stable in the presence of surfactant. Nothing in the prior art discloses the claimed compositions and methods. The novel formulations solve stability problems in accordance with the disclosure. All references are deficient and fail to describe a detergent composition or surfactant containing composition including polymersome(s) in accordance with the present disclosure. No claims are obvious in light of the cited references. Reconsideration is urged.

Claims 1 and 2 relate to detergent compositions including surfactant; and enzyme encapsulated in a polymersome including a uni-lamellar or multi-lamellar vesicle, wherein the vesicle includes at least 50% of a synthetic polymer as a vesicle forming agent, wherein the synthetic polymer is a di- or tri-block-co-polymer composed of monomers selected from the group consisting of ethyleneoxide, propyleneoxide, ethylethylene, acrylic acid and vinyl amine, and wherein the polymersome is characterized as stable in the presence of a surfactant. Claim 2 additionally requires at least two enzymes.

Claim 5 relates to a method including the steps of: (a) encapsulating at least one enzyme in a polymersome including a uni-lamellar or multi-lamellar vesicle, and (b) adding the vesicle to a surfactant containing composition, wherein the vesicle comprises at least 50% of a synthetic polymer as a vesicle forming agent; wherein the synthetic polymer is a di- or tri-block-co-polymer composed of monomers selected from the group consisting of ethyleneoxide, propyleneoxide, ethylethylene, acrylic acid and vinyl amine, and wherein the polymersome is stable in the presence of surfactant.

Claim 6 relates to a method of preventing an enzyme from reacting with other compounds in a surfactant containing composition. Claim 8 relates to a method for improving the stability of an enzyme in a surfactant containing composition. Claim 29 relates to a liquid detergent containing composition including: surfactant; and enzyme encapsulated in a polymersome in accordance with the present disclosure.

Wong is deficient as a prior art reference. Wong relates to a dispersion of uniformly sized population of multilamellar lipid vesicles (liposomes) encapsulating an aqueous liquid prepared from forming a dry film of lipids on the walls of a vessel, contacting the film with an aqueous liquid in the presence of spheres and agitating. However, Wong is deficient for failing to describe a detergent composition or surfactant containing composition including polymersome(s) which remains stable in the a surfactant containing composition. The Examiner has admitted that –What is lacking in this reference is the teaching of the use of the composition as detergent compositions. See page 4 of the Final Rejection. As Wong does not describe any vesicles in a detergent containing surfactant, Wong is deficient in failing to suggest or demonstrate vesicles in Applicants' novel compositions. Accordingly, Wong does not even attempt to solve stability problems in accordance with the present disclosure, or express the elements of claims 25-28. The Examiner alleges that Wong teaches the use of synthetic surfactants for the preparation of liposomes. Such use in creating a liposome is different than placing the final liposome product in a harsh chemical environment (containing surfactant) and solving stability problems in accordance with the present disclosure.

Meier fails to cure the deficiencies of Wong and *vice versa*. Meier relates to vesicles made from amphiphilic copolymers. The copolymers can be crosslinked to form nanocapsules. Molecules such as membrane proteins can be incorporated into the wall of the vesicles or nanocapsules. Meier further relates to incorporating molecules into the vesicles, such as for the delivery agents in a controlled delivery system. However, Meier is deficient for failing to describe a detergent composition or surfactant containing composition

including polymersome(s) in accordance with the present disclosure. The Examiner has admitted that –What is lacking in this reference is the teaching of the use of the composition as detergent compositions. See page 4 of the Final Rejection. Further, Meier is devoid of any suggestion to solve problems associated with detergent composition and surfactant, and the need for the vesicle to remain stable in the presence of a surfactant. As Meier does not describe any vesicles in a detergent containing surfactant, Meier is deficient in failing to suggest or demonstrate vesicles which are stable in accordance with the present disclosure, including the stability as specifically set forth in claims 25-28. Meier does not attempt to solve vesicle stability problems under harsh conditions such as a detergent formulation containing surfactant.

The Examiner states that "the burden is upon the applicant [to show] that the prior art polymersomes do not behave the same way as the instant polymersomes". It is inappropriate to shift the burden to the Applicants before making a *prima facie* case of obviousness. This is especially true where the Examiner has admitted –What is lacking in this reference is the teaching of the use of the composition as detergent compositions. See page 4 of the Final Rejection. The Examiner has not reasonably shown vesicles of the Meier applied in detergent compositions or surfactant containing compositions and failed to show each and every element of the novel claims. Further, the Examiner has failed to make a *prima facie* showing obviousness for the reasons herein. Reconsideration is urged.

Discher fails to cure the deficiencies of Wong and/or Meier. Discher, relates to vesicles made from amphiphilic diblock copolymers characterized by micromanipulations. Discher states that with the rich variety of phospholipids and membrane modifiers, each synthetic membrane might find its own application in transport, rheology, or encapsulation, rationally based on a suitable selection of material properties, thermal behaviors, and permeabilities. However, Discher is deficient for failing to describe a detergent composition or surfactant containing composition including polymersome(s) which remains stable in the presence of a surfactant. Further, the Examiner has admitted that –What is lacking in this reference is the teaching of the use of the composition as detergent compositions. See page 4 of the Final Rejection. As Discher does not describe any vesicles in a detergent, or in contact with a surfactant, Discher is deficient in failing to suggest or demonstrate vesicles which are stable in accordance with the present disclosure, including the stability as specifically set forth in claims 25-28. Discher does not attempt to solve vesicle stability problems under harsh conditions such as a detergent formulation containing surfactant.

WO 97/24177 relates to a liquid detergent concentrate having an outer liquid detergent phase and enzyme containing particles dispersed in the liquid phase. As previously explained on the record, WO 97/24177 is Applicant's own prior work (Applicant was formerly Novo Nordisk, the co-applicant of WO 97/24177). WO 97/24177 does not teach or even suggest compositions comprising a compound encapsulated in a vesicular encapsulation structure, as claimed in the present claims. Rather, WO 97/24177 discloses an encapsulation shell for an enzyme core which is formed by *in situ* coacervation or condensation of a monomeric or polymeric agents. See WO 97/24177 at page 5, lines 33-35, page 6, line 35 to page 7, line 5. The encapsulation layer resulting from the coacervation or condensation reaction is a randomly cross-linked (i.e., web-like or plastic-like structure), not a vesicular structure (i.e., uni- or multi-lamellar structure). Thus, WO 97/24177 clearly does not teach or suggest to employ a vesicular encapsulation layer for a compound. WO 97/24177 is deficient for failing to describe a detergent composition or surfactant containing composition including polymersome(s) which remains stable in the presence of a surfactant. As WO 97/24177 does not describe any vesicles in a detergent, or in contact with a surfactant, WO 97/24177 is deficient in failing to suggest or demonstrate vesicles which are stable in accordance with the present disclosure, including the stability as specifically set forth in claims 25-28. WO 97/24177 does not attempt to solve vesicle stability problems under harsh conditions such as a detergent formulation containing surfactant.

Accordingly, Applicants maintain that the Examiner has failed to show each and every element of the claimed invention and thus failed to make a *prima facie* showing of obviousness.

Applicants submit the level of skill is high in making detergent applications in accordance with the present disclosure. One of ordinary skill in the art would not simply combine the references and expect success.

Moreover, the Examiner has not provided reason to combine these references. At most, the combination proposed by the Examiner may offer an invitation to do experiments on vesicles and detergent compositions.

A patent claim is obvious over a combination of prior art references only when "the prior art would have suggested to one of ordinary skill in the art that [the claimed invention] should be carried out and would have a reasonable likelihood of success... . Both the suggestion and the expectation of success must be founded in the prior art, not in the applicant's disclosure." *In re Dow Chemical*, 837 F.2d 469, 473 (Fed. Cir. 1988);

see also, 35 U.S.C. § 103. An invitation to experiment, alone, cannot make an invention obvious. *In re Dow*, 837 F.2d at 473.

Applicants believe there is no evidence given by Meier, Wong, Discher or WO 97/24177 that vesicles as claimed would be suitable for use in detergent compositions. A skilled person in the art would have no reasonable expectation of success that vesicles can be used to solve the problems of the present disclosure. Even if it was obvious to try to experiment it is not necessarily true that there would be any reasonable expectation of success. In the present case, a reasonable expectation of success requires that the skilled person can predict that vesicles would solve the problems of the present disclosure in a detergent composition (e.g., a harsh environment containing surfactants). It is well known that substances that are mechanically tough often break down under certain chemical conditions.

Applicants direct the Examiner's attention to examples 1-2, showing encapsulation in vesicles of polymers and phospholipids. Vesicles were produced by ultrasound and measured to ascertain the properties of the vesicles and the amount of encapsulated enzyme. Clearly, the inventors performed a novel function and contributed to the art. Prophetic example 3 is also a contribution to the art. After all, this Example was provided by highly skilled artisans for the understanding of other skilled artisans.

Even if there were motivation to try the vesicles of Meier, Wong, or Discher in detergent composition (which Applicants do not concede is proper), there was no reasonable expectation of success because it was not predictable whether the vesicles in a surfactant containing environment as claimed would work at all. At best, some stability of the vesicle could be hoped for, possibly making it worth a try. However, an invitation to experiment cannot make an invention obvious. *Dow*, 837 F.2d at 473. Applicants have made a contribution to the art and disclosed the information available to the public.

Applicants further note that the Examiner has not provided a sufficient reason or explicit analysis of why the disclosures of the references should be combined. The cited references are devoid of any suggestion to combine the teachings and suggestions of Meier, Wong, Discher or WO 97/24177 as advanced by the Examiner, except from using Applicants' disclosure as a template through hindsight reconstruction of Applicants claim. Thus, the Examiner has erroneously retraced the path of the inventor with hindsight – discounting the number of complexities of the alternatives in order to conclude that the specifically claimed composition was obvious. This reasoning is always inappropriate for

an obviousness test based on the language of Title 35 that requires the analysis to examine "the subject matter as a whole" to ascertain if it "would have been obvious at the time the invention was made." 35 U.S.C. § 103(a). It is erroneous to equate obvious to try with obviousness under 35 U.S.C. 103 where "what was "obvious to try" was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it." See *In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988). In this case, the improvement is more than the predictable use of prior art elements according to their established functions. The improvement bolsters stability in an unpredictable and harsh chemical medium (e.g. detergent or surfactant containing medium).

The Examiner has admitted that Meier, Wong, and Discher lack any teaching of the use of the composition as detergent compositions. Even applying a non-rigid TSM analysis, there is no teaching, suggestion or motivation given by any prior art references, alone or in combination, to modify the compositions of WO 97/24177 to include vesicles in accordance with the present disclosure and somehow arrive at Applicants' invention. Thus no claim is obvious. Reconsideration is urged.

II. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

Date: April 21, 2009

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